PROPOSED RESPONSE - DO NOT ENTER

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	) Confirmation No.: 8381
	)
Noboru HORIGUCHI et al	) Art Unit: 1743
	)
Serial No.: 10/676,107	) Examiner: Wallenhorst, Maureen
	)
Filed: October 2, 2003	)
	)
For: BLOOD TESTING METHOD	)

RESPONSE TO OFFICE ACTION OF DECEMBER 7, 2006

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Responsive to the office action of December 7, 2006, please amend the captioned application as follows.

IN THE CLAIMS:

1. (Currently amended) A blood test method comprising the steps of

(a) centrifuging a mammalian blood sample into a plasma and blood cells;

(b) removing buffy coats from said blood cells to obtain red blood cells containing solutes confined therewithin;

(c) washing said red blood cells with a buffered physiological saline solution and isolating said washed blood cells;

(d) mixing said washed red blood cells with a buffered physiological saline solution to obtain a suspended liquid;

(e) centrifuging said suspended liquid to remove a supernatant and to obtain a red blood cell layer;

(f) mixing said red blood cell layer with a hypertonic solution and maintaining the resulting suspension at a temperature of 25 to 40° C for a period of time sufficient for the solutes confined in the red blood cells to penetrate into the hypertonic solution;

(g) centrifuging the suspension to obtain a supernatant containing the solutes; and

(h) measuring the supernatant for at least one factor selected from the group consisting of ~~a~~ glucose concentration, ~~a~~ pyruvic acid concentration, ~~a~~ lactic acid concentration and ~~an~~ oxidation-reduction potential.

2. (Currently amended) A blood test method as claimed in claim 1, wherein step (a) comprises centrifuging the ~~venous~~ blood sample at a force of 130x g to 200xg for 5 to 10 minutes.

3. (Original) A blood test method as claimed in claim 1, wherein step (b) comprises mixing the blood cells with a sedimentation agent, and centrifuging the resulting mixture at a force of 800xg to 1,200xg for 7 to 12 minutes.

4. (Original) A blood test method as claimed in claim 1, wherein step (c) comprises mixing said red blood cells with a phosphate buffered physiological saline solution, and centrifuging the resulting mixture at a force of 130xg to 200xg for 5 to 10 minutes.

5. (Original) A blood test method as claimed in claim 1, wherein step (d) comprises mixing said washed red blood cells with a phosphate buffered physiological saline solution in an amount so that the suspended liquid has a hematcrit value of 40 to 50 %.

6. (Original) A blood test method as claimed in claim 1, wherein step (e) comprises centrifuging the suspended liquid at a force of 130 xg to 200xg for 5 to 10 minutes, and removing the supernatant.

7. (Original)) A blood test method as claimed in claim 1, wherein step (f) comprises mixing the red blood layer with a 5 to 10 % weight saline solution and maintaining the resulting mixture at a temperature of 35 to 38° C for 7 to 15 minutes.

8. (Original) A blood test method as claimed in claim 1, wherein step (g) comprises centrifuging the suspension at a force of 1,500xg to 2,000xg for 7 to 12 minutes.

9. (Currently amended) A blood test method as claimed in claim 1, wherein step (h) comprises measuring the supernatant for at least one factor selected from the group consisting of ~~a~~ glucose concentration, ~~a~~ pyruvic acid concentration and a lactic acid concentration using an automatic biochemical analyzer.

10. (Original) A blood test method as claimed in claim 1, wherein step (h) comprises measuring the supernatant for an oxidation-reduction potential using a potentiometer.

11. (New) A blood test method as claimed in claim 1, wherein said at least one factor includes glucose concentration.

12. (New) A blood test method as claimed in claim 11, further comprising:

evaluating glucolysis in the red blood cells on the basis of results of said measuring.

13. (New) A blood test method as claimed in claim 1, wherein, said at least one factor includes oxidation-reduction potential and further comprising:

measuring the oxidation-reduction potential of the plasma; and

determining if the measured oxidation-reduction potential of the plasma and the measured oxidation-reduction potential of the supernatant fall within standard ranges.

14. (New) A blood test method as claimed in claim 1, wherein said at least one factor includes lactic acid concentration and further comprising:

measuring lactic acid concentration in the plasma;

comparing lactic acid concentration in the supernatant with lactic acid concentration in the plasma; and

evaluating metabolism of the red blood cells based on the results of the comparison.

REMARKS

Claims 1, 2 and 9 have been amended to address the rejection for indefiniteness which is considered to be now moot.

New claims 11-13 find support in the description of the working examples at pages 9-15. New claim 14 finds support in the form of a corresponding description at page 12 of applicants' specification.

The rejection of claims 1-10 for obviousness over GB Patent No. 996,089 in view of Barrett-Reis et al is respectfully traversed because: (1) the rejection appears to be based on an erroneous interpretation of GB '089; (2) temperatures within the range of 25-40° C are unsuitable for use in the blood preservation method of GB'089 and (3) the combination of the teachings of Barrett-Reis with the blood preservation method of GB'089 is improper.

Interpretation of GB'089

In the paragraph spanning pages 3 and 4 of the office action the Examiner seems to be combining teachings of GB'089 relating to two very different methodologies with the result being some type of blend that bears little or no resemblance to any methodology taught or suggested by GB'089.

The first methodology disclosed by GB'089 can properly be described as involving blood tests to determine levels of lactic acid in the blood. See page 1, line 78 to page 2, line 32. These tests were conducted to determine why the storage time of erythrocytes at 4o C in actual practice was "less than 30 days" whereas the theoretical storage time of erythrocytes at 4o C projects to 1200 days based on the levels of lactic acid obtained from blood samples incubated at various temperatures as shown in Fig. 1. See page 1, line 83 to page 2, line 9. The invention of GB'089 is based on the discovery that, while the rate of the metabolic reactions that give lactic acid falls with drop in temperature, the "speed of movement of the toxic metabolic products through the cell walls drops considerably faster than the velocity of the metabolic reactions," quoting from page 2, lines 11-15. Note that no clue is given as to the nature of the

assay for lactic acid, other than it can be "directly" applied to measure metabolic products within the red blood cells. See page 2, lines 25-32.

The second method taught by GB'089, while based on the foregoing discovery, does **not** involve measurement of levels of lactic acid and is not a blood test at all. This second method is a method of blood preservation in which "at least a portion of the intracellular metabolic products of the erythrocytes (e.g. lactic acid) is removed from the erythrocytes during storage and/or intercepted inside the erythrocytes," quoting from page 2, lines 47-51. One embodiment of the invention involves "feeding appropriate adsorbents in suitable quantity to the blood to be stored," quoting from page 2, lines 69-71. In another embodiment, apparently referred to by the Examiner, the blood is stored in "containers made of a material which is permeable to low-molecular weight substances, that is, the products of metabolism, such as semipermeable membrane," quoting from page 2, lines 75-79. In the latter embodiment continuous dialysis is used to remove the metabolic products from the stored blood. GB'089 does not teach or any blood preservation method of the invention would involve any type of test for lactic acid.

Thus, it seems that the examiner has improperly somehow blended a teaching relating to testing that provided the theoretical background of the invention with a description of the invention itself, which is not a blood test.

Test Temperature

At page 4 of the office action the Examiner writes:

> "Therefore, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to maintain the erythrocytes in the suspension medium [the preservation method] taught by the GB patent in a temperature range of 25-40° C since Figure 3 of the GB patent [the experimental background] depicts that this temperature range promotes the diffusion of metabolic products such as lactic acid from the interior of the erythrocytes to the exterior, extracellular suspension medium, thus helping to eliminate the deleterious affects caused by these metabolic products."

Again, the Examiner is improperly combining teachings relating to different concepts. Further, while increasing the temperature would speed diffusion of the metabolic products through a membrane it would also speed up the metabolic reactions. It is respectfully submitted that those skilled in the art would not attempt to store blood at 25-40° C. As shown by the attached, blood is stored either frozen or at a refrigerated temperature of about 4° C. GB'049 contemplates refrigerated storage at 4° C - see page 2, lines 4-6 and the teaching of use of a refrigerator at page two, lines 104-110. One would not use a refrigerator to maintain temperatures above room temperature, e.g. temperatures within the range of 25-40° C.

The Propriety of Combining Barrett-Reis with GB'089

Barrett-Reis et al disclose isolation of red blood cells and plasma, not a storage method. Accordingly, Barrett-Reis cannot properly be characterized as suggesting any modification of a method of blood storage.

New Claims 11-14

No reference of record teaches or suggests any method for measuring glucose concentration (claims 11 and 12), any blood test involving measurement of oxidation-reduction potential in red blood cells and/or plasma (claim 13) or any method involving separate measurements of lactic acid concentrations in the red blood cells and in the plasma and a comparison of those measurements.

In conclusion, the Examiner is respectfully requested to reconsider and withdraw the rejections of record.

Respectfully submitted,

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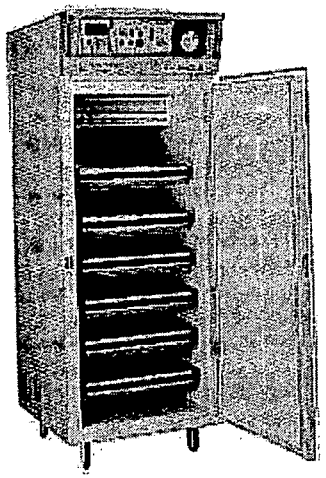
SO-LOW

Blood Storage Refrigerators/Freezers

SETTING THE STANDARD IN EVERY LAB

- Home Page
- Freezers to -85?C
- Freezers to -40?C
- Freezers to -20?C & -25?C
- Inventory Systems
- Accessories
- Lab & Pharmacy Freezers
- Lab & Pharmacy Refrigerators
- Blood Storage Refrig. / Freezers
- Chromatography Refrig.
- Flammable Material Storage
- Explosion Proof /Manual Defrost
- Undercounter Freezers / Refrig.
- Incubators / Ovens / Furnaces
- Waterbaths /Hotplates /Stirrers
- LN2 Cryogenic Storage Systems
- Walk-In Rooms
- Humidity Stability Chambers



- ALARM SYSTEM - features audio and visual signal for high and low temperature, door ajar, power loss, battery backup and remote contacts.
- TEMPERATURE RECORDER - offers a 6" dial, 7-day clock with stylus pen.
- CFC-FREE - refrigerant and insulation
- UL LISTED

- KEY ON/OFF SWITCH - for secure operation
- LCD TEMPERATURE READOUT - highly visible and a displaying ?C scale in tenths of a degree. Easy to read ang panel.
- CABINET WALLS - made of 22 gauge cold roll steel (ex gauge galvanized steel (interior) for lasting durability. Bo finished with high luster baked-enamel coatings. Insulatio 3/8" (6cm) foamed-in-place urethane (CFC-Free) for mor temperature control.
- DOUBLE-PANED TEMPERED GLASS DOORS - are t controlled for reliable self closing. Keylocks provide adde
- 40-WATT FLUORESCENT INTERIOR LIGHT - provid lighting. External power control switch on control panel(s
- DRAWERS - 6" Cantilever, 100% pullout, ball bearing
- 6" (15.2 cm) ADJUSTABLE LEGS - allow you to easily cabinet and make accommodating height adjustments.
- ADJUSTABLE THERMOSTAT
- EXPANSION VALVE REFRIGERANT CONTROL
- FIN & TUBE FORCED AIR CONDENSER/EVAPORA
- CYCLE DEFROST - defrost coils whenever the compres running. No heater or timer necessary.

Note: All units meet the standard requirements of the A.A.B.B.

General Specifications

BLOOD STORAGE REFRIGERATORS				
MODEL NO.	CU. FT	TEMPERATURE RANGE	INTERIOR DIMENSIONS, INCHES, (CM) W x F-B x H	EXTERIOR DIMENSION INCHES (CM) W x F-B x
DHN4-5UCBBR	5	4?C	23" x 19.5" x 22.88" (58 x 49 x 58)	27" x 25" x 34" (68 x 63 x 86)
DHN4-24BBR	24	1?C to 6?C	23.5" x 30" x 59" (59 x 76 x 150)	27.5" x 35.5" x 81.50" (69 x 90 x 207)
DHN4-52BBR	52	1?C to 6?C	51" x 30" x 59" (129 x 76 x 150)	55" x 35.5" x 80.375" (139 x 90 x 204)
BLOOD STORAGE FREEZERS				
DHN30-5UCBBF	5	-30?C	23" x 19.5" x 22.88" (58 x 49 x 58)	27" x 25" x 34" (68 x 63 x 86)
DHN30-21BBF	22.5	-30?C	23.5" x 28" x 59" (59 x 71 x 150)	27.5" x 34.875" x 82.75" (69 x 88 x 210)
DHN30-48BBF	48.8	-30?C	51" x 28" x 59" (129 x 71 x 150)	55" x 34.875" x 84.625" (139 x 88 x 215)

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Blood Storage Refrigerators / Freezers | Chromatography Refrigerators | Flammable Material Storage
Explosion Proof / Manual Defrost | Undercounter Freezers / Refrigerators | Incubators / Ovens / Furnaces
Waterbaths / Hotplates / Stirrers